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Long-term non-surgical control with ulipristal acetate of multiple uterine fibroids, enabling pregnancy

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Condensation:

MR images depict a marked response to Ulipristale Acetate in a woman with large uterine fibroids, and demonstrate no significant regrowth during pregnancy or 12 weeks postpartum.

Short Title: UPA non-surgical fibroids control

Case note: A 39-year-old woman under our care for five years for multiple uterine fibroids presented requesting a review of her condition with a view to attempting pregnancy. Previous treatment included laparotomic myomectomy in 2006, GnRH agonist therapy (monthly leuprolide acetate injections in the PEARL II study[1]) in 2008, and hysteroscopic myomectomy in 2009, and had been asymptomatic on desogestrel treatment for 1 year. On clinical examination, uterine volume was equivalent to 20 weeks' gestation and magnetic resonance imaging (MRI) revealed multiple, disseminated, diffuse myomatosis (Figure A). Treatment was initiated with 5 mg oral ulipristal acetate (UPA) daily. MRI evaluation showed a significant decrease in fibroid volume after 3 months, continuing after 6 months (Figures B, C). Without surgery, the patient proceeded with in vitro fertilization for andrologic concern and age. Pregnancy was confirmed following her first embryo transfer, 11 months after beginning and 3.5 months after ending UPA treatment. No significant fibroid regrowth was noted at MRI performed during pregnancy (Figures D, E). Because of previous laparotomy with myomectomy, cesarean section was planned and a healthy baby was delivered at 39 weeks. Follow-up MRI 12 weeks after delivery showed sustained regression of the myomas, both in number and size, also due to 'natural' remodeling after pregnancy[2] (Figure F). The patient remains asymptomatic one year post-delivery.

Comment: This MRI-based analysis of UPA treatment for diffuse uterine myomatosis reveals an unprecedented level of effectiveness, sustained even throughout the subsequent pregnancy. However, fibroid response to UPA in terms of volume reduction is very unpredictable[3]. Courtoy et al. conducted immunohistochemistry, microarrays and histology studies on surgical specimens and described a multifactorial mechanism of action[4]: UPA increased apoptosis of myoma cells, but only at the beginning of treatment, by a pathway independent of the caspase. After long-term treatment with UPA, modification of the extra-cellular matrix (ECM) was significant compared to the untreated group, with an increase in matrix

metalloproteinase 2 (MMP-2) levels. Hence, in patients showing such a marked response to UPA treatment, it is possible that pregnancy could continue to modify the ECM by uterine growth. The remaining fibroid cells may have been selected by primary UPA-mediated apoptosis resulting in a population of cells less sensitive to hormonal stimulation, due to modification of progesterone receptor expression, as shown for other selective progesterone receptor modulators[5].

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Figure: *MRI images showing regression of uterine fibroids during UPA treatment and subsequent pregnancy*
Multiple large myomas (dark ovals) and a distorted and reduced-capacity uterine cavity (light area) were visible before treatment (A). Subsequent MRIs showed successive improvements after 3 months (B) and 6 months (C) of UPA; with no significant regrowth during early pregnancy (D, 13 weeks' gestation). Further shrinkage was observed in the third trimester (E, 32 weeks' gestation), with disappearance of most fibroids by 12 weeks after delivery (F).

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